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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,362	06/25/2005	Cosimo De Bari	50304/030001	8489

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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/522,362	DE BARI ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 36-54* is/are pending in the application.

4a) Of the above claim(s) *43-52,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,36-42 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/27/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed on 2/06/2006 has been entered.

2. Applicant's election with traverse of the invention of group I (claims 1, 36-42 and 53) filed on February 6, 2006 is acknowledged. Applicant's declaration and arguments filed 2-6-2006, have been fully considered and references applied to show lack of unity for the restriction requirement has been withdrawn. However, applicant's argument that all the groups should be examined is not persuasive because the special technical feature as recited in the claim 1 was known in the prior art. For example, De Angelis et al (The Journal of Cell Biology, 1999, 147(4), 869-878) teach cells derived from embryonic vessel can give rise to skeletal myogenic cells. It is noted that these myogenic cell show morphology similar to satellite cells *in vitro* and *in vivo*. Therefore, the linking feature of a composition comprising a population of mammalian muscle progenitor cells was know in the art at the time of filing of this application and thus instant application lacks technical feature linking the recited groups as would be required to fulfill the requirement for unity of invention. Additionally, the invention of groups II-III lacks the same technical feature as of group I because the technical feature of group I is a progenitor cell while technical feature of treatment method of group II will be based on specific condition whereas group III requires specific antibody for selecting specific cell population. Thus, invention of group II and III have their own inventive concept as described in previous office action (pp 3, para 3).

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 43-52 and 54-55 (groups II and III) have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 6, 2006.

4. Claims 1, 36-42 and 53 are pending.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 37-38 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37 and 38 are vague and indefinite because they recite any marker co expressed or co detected with disclosed positive and/or negative markers. The term "any marker" as recited in the claim in view of teaching in the specification render instant claims indefinite as meets and bounds of the claim cannot be determined.

Claim 42 is vague and indefinite because the limitation fails to further limit the subject matter of claim 1. The meets and bound of the claim cannot be determined.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1, 36-39, 41-42 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by De Angelis et al (The Journal of Cell Biology, 1999, 147(4), 869-878).

Claims 1, 36-39, 41-42 and 53 are product by process and method of using product claims. Claim 1 is directed to a composition comprising a population of mammalian muscle progenitor cells derived from joint tissue, wherein the cell is myogenic in vivo and provides satellite cells when introduced into mammal. Claim 36 limit the cells derived from synovial membrane. Claims 37 and 38 further characterize cell population by positive and negative markers. Claim 39 limits the cells of claim 1 to include genetically engineered cells. Claim 41 limits the composition of claim 1 to

include clonal cells. Subsequent claim limits the cell to be an isolated and passaged cell.

De Angelis et al teach presence of clonable skeletal myogenic cell in embryonic dorsal aorta (abstract). De Angelis et al disclose mouse satellite cells grown in culture under clonal conditions expressing myogenic markers can be differentiated into multinucleated myotubes upon mitogen deprivation. It is noted that De Angelis et al describe limbs from E13 or E11 that are pre cultured as explants and then dissociated to a single cell suspension and cultured at low density. These myogenic clones are consistent with satellite cells phenotype (Figure 2) (pp 870, col. 2, para 2). De Angelis et al also compare the phenotype of clonable satellite like cell. It is noted that most of the myogenic markers (c-met) are expressed by these clones (table 1, Figure 4). It is emphasized that the composition of De Angelis will be same after 3 passages, therefore, passage number is not limiting to the disclosed composition. In addition, De Angelis suggests potential of these cells for *in vivo* myogenic differentiation by genetically modifying myogenic progenitor cells to express LacZ (pp 870, col. 2, para 1). De Angelis discloses genetically labeled nuclei of the cell from dorsal aorta are incorporated into newly formed muscle fibers of SCID/bg mice. Accordingly, because De Angelis teach the isolation of clonal cell that is myogenic *in vivo* and provide satellite cells phenotype that expresses a marker encompassed by claims, these would be inherently be cells that would provide persistent pool of satellite cell.

Where, in the instant case, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes,

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)). Further see MPEP § 2113, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (Citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

9. Claims 1, 36-39, 41-42 and 53 and are rejected under 35 U.S.C. 102(a) as being anticipated by Qu-Petersen et al (The Journal of Cell Biology, 2002, 157(5), 851-864).

Claims 1, 36-39 and 41-42 are product by process and method of using product claims. Claim 1 is directed to a composition comprising a population of mammalian muscle progenitor cells derived from joint tissue, wherein the cell is myogenic in vivo and provides satellite cells when introduced into mammal. Claim 36 limit the cells derived from synovial membrane. Claims 37 and 38 further characterize cell population by positive and negative markers. Claim 39 limits the cells of claim 1 to include genetically engineered cells. Claim 41 limits the composition of claim 1 to include clonal cells. Subsequent claim limits the cell to be an isolated and passaged cell.

Qu-Petersen et al teach isolation and culture of muscle-derived stem cell (MDSC) that could divide for more than 30 passages while preserving their normal karyotype (abstract). It is noted that Qu-Petersen et al show of CD34 expression of MDSC at passage 10 (Figure 3), while a sub clone culture displayed 91% of the cells were CD34 with similar phenotypes. Qu-Petersen et al also disclose MDSC cells with a retrovirus carrying the *lacZ* reporter gene to determine the self-renewal capacity of MDSC *in vivo* (pp 855, col.1 last line and Figure 3). The results show 10 times more dystrophin^{+} myofibers in MDSC-injected groups after 30 and 90 d post transplantation suggesting that the MDSC possess a high capacity for long-term proliferation *in vitro* and *in vivo* by replenishing satellite cell compartment in the injected skeletal muscle (pp 855, col. 1, para 1 and 2). It is emphasized that Qu-Petersen et al specifically teach a

method of providing a persistent reserve population of satellite cell in mice by directly injecting the cell composition to the mice.

Accordingly, because Qu-Petersen et al teach the isolation of clonal cell that is myogenic *in vivo* and provides satellite cell that expresses a marker encompassed by instant claims upon transplantation in mice, these would be inherently be cells that would also express other positive and negative markers as recited in the instant application.

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or obtain and compare prior art products...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)). Further see MPEP § 2113, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695,

698, 227 USPQ 964, 966 (Fed. Cir. 1985) (Citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

10. Claims 1 and 39-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Chancellor et al (US Patent no 6866842, dated 3/15/2005, effective filing date 5/1/1998).

Claims 1, 39-40 are product by process claims.

Chancellor et al teach a muscle-derived cells, preferably myoblasts and muscle-derived stem cells that is genetically engineered to contain and express one or more heterologous genes for delivery of the encoded gene products at different sites (abstract). It is noted that Chancellor et al disclose injecting autologous muscle-derived cells (e.g., myoblasts, and muscle-derived stem cells (MDCs)) that have been transfected or transduced with a vector containing at least one gene encoding a growth factor (bFGF, IGF-1, VEGF, PDGF A, B, BMP-2, CDMP) or a neurotropic factor, into a muscle tissue (col. 9, lines 27-32). Chancellor et al show that Myoblast transplantation comprising implantation of myoblast precursors (satellite cells) enhances muscle

regeneration and creates a reservoir of normal myoblasts that can fuse and deliver genes to skeletal muscle (col. 48, lines 42-45). It is also disclosed that intra-articular injection of genetically engineered muscle cells adhered to several structures in the joint, including the ligament, capsule, and synovium. In addition, myoblasts fused to form many post-mitotic myotubes and myofibers at different locations of the newborn rabbit (col. 49, lines 7-16) suggesting these precursor cells are satellite cells.

Accordingly, Chancellor et al anticipate claims 1 and 39-40.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1, 36-42 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Angelis et al (The Journal of Cell Biology, 1999, 147(4), 869-878)

and Chancellor et al (US Patent no 6866842, dated 3/15/2005, effective filing date 5/1/1998).

De Angelis et al teach presence of clonable skeletal myogenic cell in embryonic dorsal aorta (abstract). De Angelis et al disclose mouse satellite cells grown in culture under clonal conditions expressing myogenic markers can be differentiated into multinucleated myotubes upon mitogen deprivation. It is noted that De Angelis et al describe limbs from E13 or E11 that are pre cultured as explants and then dissociated to a single cell suspension and cultured at low density. These myogenic clones are consistent with satellite cells phenotype (Figure 2) (pp 870, col. 2, para 2). De Angelis et al also compare the phenotype of clonable satellite like cell. It is noted that most of the myogenic markers (c-met) are expressed by these clones (table 1, Figure 4). It is emphasized that the composition of De Angelis will be same after 3 passages, therefore, passage number is not limiting to the disclosed composition. In addition, De Angelis suggests potential of these cells for *in vivo* myogenic differentiation by genetically modifying myogenic progenitor cells to express LacZ (pp 870, col. 2, para 1). De Angelis discloses genetically labeled nuclei of the cell from dorsal aorta are incorporated into newly formed muscle fibers of SCID/bg mice. Accordingly, because De Angelis teach the isolation of clonal cell that is myogenic *in vivo* and provide satellite cells phenotype that expresses a marker encompassed by claims, these would be inherently be cells that would provide persistent pool of satellite cell. However, De Angelis et al do not teach genetically modifying cells with peptide growth factor or angiogenic growth factors.

Chancellor et al teach a muscle-derived cells, preferably myoblasts and muscle-derived stem cells that is genetically engineered to contain and express one or more heterologous genes for delivery of the encoded gene products at different sites (abstract). It is noted that Chancellor et al disclose injecting autologous muscle-derived cells (e.g., myoblasts, and muscle-derived stem cells (MDCs)) that have been transfected or transduced with a vector containing at least one gene encoding a growth factor (bFGF, IGF-1, VEGF, PDGF A, B, BMP-2, CDMP) or a neurotropic factor, into a muscle tissue (col. 9, lines 27-32). Chancellor et al show that Myoblast transplantation comprising implantation of myoblast precursors (satellite cells) enhances muscle regeneration and creates a reservoir of normal myoblasts that can fuse and deliver genes to skeletal muscle (col. 48, lines 42-45). It is also disclosed that intraarticular injection of genetically engineered muscle cells adhered to several structures in the joint, including the ligament, capsule, and synovium. It is emphasized that Chancellor et al teach healing of muscle; meniscal injuries and other muscle related disorder could be improved by cell mediated delivery of exogenous gene for the expression of gene product (Col. 8, lines 7-10; col.8, lines 40-46 and 61-64).

It would have been obvious for one of ordinary skill in the art at the time of invention to modify the composition of De Angelis by genetically modifying the composition by exogenously incorporating nucleic acid encoding growth factor as described by Chancellor. Chancellor et al had already disclosed a muscle-derived stem cells (MDCs) that have been transfected or transduced with a vector containing at least one gene encoding a growth. In addition, Chancellor et al had taught the importance of

delivering genetically modified cell for healing meniscal injuries and other muscle related disorder (Col. 8, lines 7-10; col.8, lines 40-46 and 61-64). The skilled artisan would have been motivated to modify the composition of De Angelis to incorporate nucleic acid comprising growth factor as described by Chancellor to improve the healing of muscle injury by delivering cells comprising exogenous genes for the expression of gene product at the injury site.

One who would have practiced the invention would have had reasonable expectation of successfully obtaining a composition comprising a genetically engineered population of mammalian muscle progenitor cell having *in vivo* myogenic activity because De Angelis already taught a composition comprising mammalian muscle progenitor cell have *in vivo* myogenic property and Chancellor had described the importance of genetically modifying muscle stem cell composition for the treatment of muscle injuries. One of ordinary skill in art would have been motivated to combine the teaching De Angelis and Chancellor because a composition of muscle progenitor cell comprising a promoter operably linked to a nucleotide sequence encoding a growth factor would have provided a progenitor cell that would have been useful in the treatment for various muscle disorder as taught by Chancellor.

Therefore, the claimed invention would have been prima fascia obvious to one of ordinary skill in the art at the time of the invention.

10. No Claims allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 8:30AM-5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272- 0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Anoop Singh, Ph.D.
Examiner, AU 1632

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER